Type 2 Diabetes Update: Semaglutide and Linagliptin as Basal Insulin Alternatives

By Christine Kilgore

Cardiovascular comorbidities and risk reduction play a major new role in pharmacologic therapy for type 2 diabetes, with sodium-glucose transporter 2 (SGLT2) inhibitors and glucagon-like peptide 1 (GLP-1) receptor agonists now recommended as part of the glucose-lowering regimen for patients who have established atherosclerotic cardiovascular disease (ASCVD) or indicators of high-risk, chronic kidney disease (CKD) or heart failure (HF).

"We should always assess patients now in that light, asking whether they have a stent, a [history of] stroke, a transient ischemic attack, or any vascular procedure, for instance, because now we have the option — especially if they have heart failure or a cardiovascular complication — to use an SGLT2 inhibitor or a GPL-1 receptor agonist," said Naushira Pandya, MD, FACP, CMD, professor and chair of the Department of Geriatrics at the Kiran Patel College of Osteopathic Medicine at NOVA Southeastern University in Fort Lauderdale, FL, at the Annual Conference of AMDA – The Society for Post-Acute and Long-Term Care Medicine.

Dr. Pandya commented on the 2020 Standards of Medical Care of the American Diabetes Association (ADA) during a broad discussion of type 2 diabetes management (*Diabetes Care* 2020;43:S98–S110). The two groups of agents can be safely used in older adults if carefully selected. They have been shown to improve cardiovascular outcomes, "so they'll take a more central place in our selection of drugs and management of diabetes," Dr. Pandya said.

SGLT2 inhibitors are oral agents, and they are recommended by the ADA when HF or CKD predominates. The established GLP-1 receptor agonists (e.g., liraglutide) are injectables, and they are advised when ASCVD predominates. The Food and Drug Administration's approval last year of semaglutide, an oral GLP-1, is a "revolutionary change," and it is an option worth considering for long-term care residents, depending on cost and the needs of the patient, Dr. Pandya said during a question-and-answer period. "I personally don't have experience with it [yet], but I have patients who refuse injections and have poor control and have maxed out on three oral agents, so in that kind of person, yes [I'd consider using it]," she said. "There is some evidence for improved cardiovascular outcomes."

In fact, GLP-1 receptor agonists are now the recommended next step instead of basal insulin in patients with type 2 diabetes who need greater glucose lowering than can be obtained with two or three oral agents, Dr. Pandya said in her presentation. This new recommendation in the ADA's 2020 Standards represents "a major change in direction in the last year or so for diabetes treatment, and I think that it can apply to our settings," she said. "In the past we would have reached for basal insulin. Now, this is the way to advance your therapy."

Metformin remains the preferred initial treatment, and "it should be kept on board even as you're adding other agents," Dr. Pandya said. For people with ASCVD, CKD, or HF, a SGLT2 inhibitor or GLP-1 receptor agonist should be considered as an add-on independently of A1C goals. If not, other oral agents should be added on if the A1C is above individualized targets, with choices guided by clinical and functional status, personal preference, and sometimes cost.

Medication regimens should be reevaluated every three to six months, the ADA advises, with a focus on safety and simplification as well as intensification of treatment for patients who are not meeting treatment goals. "Remember, you're going to look at glucose trends" rather than adjusting treatment regimens in response to isolated abnormal values, said Dr. Pandya.

Some oral agents have comparable glycemic control to basal insulin, she said, sharing her own tips for managing medications with a focus on safety and simplification. In an "elegant" long-term care/skilled nursing facility study published in 2018 in *JAMDA* (2018;19:399–404.e3), linagliptin, a dipeptidyl peptidase-4 (DPP-4) inhibitor, was shown to offer comparable glycemic control with significantly lower rates of hypoglycemia compared with insulin glargine. Use of the agent does not require a renal dose adjustment.

"If you're using a small dose of basal insulin, think of stopping that and using linagliptin," she said. The drug may also be considered as an add-on agent to oral agents and basal insulin (when it's needed), especially in patients with renal insufficiency.

Sulfonylureas are "taking a bit of a back seat," Dr. Pandya noted. When sulfonylureas are used, glyburide should be avoided, and glimepiride or glipizide, which are primarily eliminated by the liver, should be used.

In a separate presentation on approaches to type 2 diabetes, Robert Accetta, RPh, BCGP, C-MTM, of Rivercare Consulting in the greater New York City area, said that the DPP-4 enzyme inhibitors have a weight-neutral glycemic benefit and are being increasingly prescribed in the community. "You may see more of these," he said, among patients coming into post-acute care. "They're now becoming a standard of practice.".

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Simplifying Insulin Management

Decreasing the burden of multiple insulin injections and blood glucose checks — and reducing the risk of hypoglycemia — has long been a goal in LTC, and it is addressed in the 2020 ADA guidelines with an algorithm on simplifying complex insulin regimens for older patients with type 2 diabetes. The algorithm proposes titrating the dose of basal insulin to a fasting blood glucose goal of 90–150 mg/dL (5–8.3 mmol/L) and adjusting mealtime insulin regimens, Dr. Pandya said.

If the mealtime dose is <10 U/dose, one can discontinue mealtime insulin and add a noninsulin agent. "Try to stop mealtime insulin if you're using just 4, 6, or 8 units," she said. If the mealtime dose is >10 U/dose, one could change mealtime insulin by first reducing the dose by 50% and adding a noninsulin agent, then continuing to titrate the dose of mealtime insulin down as the noninsulin agent is increased.

"The other thing we can do [to simply insulin management] is consider the use of a second-generation basal insulin such as degludec 200 U/mL or glargine 300 U/mL in those requiring high doses of basal insulin or who have wide fluctuations in glucose levels or hypoglycemia," she said. "There seems to be less nocturnal and overall hypoglycemia [with such a change]."

The ADA's algorithm for insulin regimen simplification incorporates the findings of a study described in 2016 in *JAMA Internal Medicine* (176:1023–1025), in which older adults receiving two or more insulin injections a day transitioned to once-a-day basal insulin glargine with or without noninsulin agents. Hypoglycemia decreased without compromising glycemic control.

To transition away from sliding-scale insulin (SSI) — another goal in PALTC — start by replacing it with basal insulin at about 50% to 75% of the total daily requirement, Dr. Pandya advised. "And if there's an existing basal insulin dose, add about 50% to 75% of the SSI total daily dose to that basal insulin dose."

Although short-term SSI may be needed for acute illness — and is often used in the hospital setting — it is neither effective nor efficient in the LTC setting in patients who are stable. The Choosing Wisely initiative — a project begun in 2012 to raise awareness of unnecessary tests and procedures across specialties — incorporates the Society's recommendation to not use SSI for long-term diabetes management in nursing homes (www.choosingwisely.org).

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risk management, and health system management.

In their study, Dr. Hirdes and his team used interRAI, a comprehensive assessment of strengths, preferences, and needs of varying populations. They found that interRAI assessments could estimate the prevalence of major COVID-19 mortality risk across care settings. For instance, in four different care settings, people with pneumonia have higher mortality rates than those without pneumonia. The mortality rates increase with major comorbidity count for individuals both with and without pneumonia, but the mortality effect is magnified within the pneumonia group.

In addressing COVID-19, Dr. Hirdes suggested that each setting has unique challenges, but most settings were not equipped to manage the challenges posed by the pandemic.

In a panel discussion on COVID-19 in AL during this session, Kevin O'Neil, MD, CMD, chief medical officer at Affinity Living Group, said, "We had infection control measures which we implemented, and we quickly established a COVID policy." He added, "Staff is knowledgeable about isolation procedures, and we have prioritized PPE [personal protective equipment] for those providing care to infected residents. We have implemented social distancing for everyone, including staff; and we've terminated group activities."

Affinity has been very careful about new admissions, and they aren't sending residents with symptoms to the hospital until they have distressed breathing. At the time of the Annual Conference, the community had one resident who had tested positive; that person was in isolation and doing well. Nonetheless, Dr. O'Neil said, "We are advising our teams not to get complacent. We are reinforcing the importance of aggressive measures every day. At the same time, we are urging staff to practice self-care, eat well, and get adequate sleep. It's critical to pay attention to our teams." He also stressed, "I'm communicating with practitioners and asking them to let me know if they have challenges or concerns. Communicating with people who have clinical expertise is essential."

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